REMARKS

By virtue of the signature affixed hereinbelow, the undersigned avers having the authority to represent Applicants and the Assignee in the above-captioned application under 37 C.F.R. § 1.34(a).

To advance prosecution, Applicants have cancelled, without prejudice to prosecution in a division application, the non-elected claims, which had been withdrawn from consideration.

The sole rejection in the instant application is of all of the pending claims, 73 and 80-106, under 35 U.S.C. § 103 over U.S. Patent No. 5,380,830 ("the '830 patent") in view of WO 99/15641 ("the PCT") and U.S. Patent No. 5,554,524 to Temin.

On page 4 of the Office Action, first full paragraph, last two sentences, the Examiner stated that there is nothing in the '830 patent and the Gonda et al. Virus Research 1994 article submitted previously and of record, that would indicate extrapolating information from HIV will not work with BIV. The Examiner stated that on reading the '830 patent, the artisan would not have been discouraged from using BIV as a vector because the ordinary artisan would not have thought that BIV would behave unpredictably.

Respectfully, the rejection is traversed for the following reasons.

Regarding the '830 patent, column 1, lines 24-28 teach that BIV is genetically distant from all other lentiviruses. Column 15, lines 16-19 of the '830 patent teach that positive cross nucleic acid hybridization of BIV and HIV was found only in pol. Also in column 15, lines 22-26, when gag and pol ORF's of BIV were compared to those of

other lentiviruses, only a low degree of homology was found. Thus, the majority of the lentivirus genes, LTR's, gag, env and the accessory genes of HIV and BIV, are dissimilar. As to the observed immunologic cross reactivity, that is explained by a short 10 amino acid stretch in p26, presumably the cross reacting determinant. The remainder of column 15 through the end of column 18 of the '830 patent summarizes further comparisons between BIV and other lentiviruses at other sites in the genomes, revealing relatively low levels of homology.

In the sentence bridging columns 19 and 20, the '830 patent speculates that BIV may be a model for HIV. That clearly is no more than an invitation to experiment as there is no teaching or guidance on which portions of the genome to manipulate, how to manipulate those portions and how to obtain infection and transgene expression in human cells with a reasonable expectation of success.

Thus, when considering the '830 patent as a whole, there is no suggestion of making BIV vectors. Moreover, there are several instances where the '830 patent teaches that BIV is genetically distinct from other lentiviruses. Finally, there is no teaching or guidance offered in the '830 patent on how to make a BIV vector that expresses a transgene in human cells with a reasonable expectation of success. Therefore, there is a clear teaching that extrapolating from FIV to BIV would not work. The differences between FIV and BIV speak to unpredictability in making a BIV vector.

With respect to WO 99/15641, in that reference as well are statements that would give an artisan pause in making a BIV vector. The PCT application relates primarily to FIV and there is a clear teaching that extrapolating from FIV to BIV is unlikely to work because of the genetic distance between the two viruses, the many factors that can deter from efficient transgene expression in human cells, and the overall unpredictability in the art.

On page 3, third full paragraph, the PCT application teaches that the use of non-primate lentiviruses is complicated by the relative lack of knowledge about their molecular properties. All lentiviruses display restricted tropism and the adaptability of such viruses to non-host animal cells is unpredictable.

In the first full paragraph on page 5 of WO 99/15641, the PCT teaches that many non-primate lentiviruses cannot establish an infective state in non-host cells. Restrictions in human cells make the use of non-primate lentiviruses therein very limited. The basis for the inability of the non-primate viruses to establish an infective state in a non-host cell, and particularly a human cell, is not known and may relate to impediments at any of a variety of steps including, entry into the cytoplasm, reverse transcription, translocation into the nucleus, integration and gene expression. Thus, the derivation of efficient vectors from non-primate lentiviruses cannot be considered predictable, as will be supported by the discussion on other lentiviruses below.

In the paragraph bridging pages 59 and 60, the PCT teaches that lentivirus encapsidation signals are very complex. That complexity contributes to a high level of unpredictability as to the reasonable expectation of successfully making a useful vector from a non-primate lentivirus, and having that vector infective in a non-host cell, such as a human cell.

Thus, it can be seen that while the PCT does mention BIV, within the same document, there is ample teaching that the results with FIV should not provide a reasonable expectation that those teachings can be extrapolated to BIV and that vectors can be made from BIV, because of the lack of knowledge of BIV and the genetic distance amongst the various viruses. The PCT provides ample evidence to conclude that an artisan would believe that vectors from BIV could not be made because of the unpredictability in the art.

Hence, at best, the published PCT application, as a whole, provides no more than an invitation to experiment because, and as will be discussed further below, there is no reasonable expectation of successfully obtaining a BIV vector, based on the results with FIV, which can efficiently express a transgene in a human cell.

That conclusion is supported by Gonda et al., Virus Research, 32:155-181 (1994), of record, which provides a summary of the biology of BIV. As noted in Fig. 2 of the Gonda et al. review, copy provided attached hereto for the convenience of the Examiner, BIV is not closely related at all to HIV, FIV, Visna or CAEV. Those viruses are more closely related to each other, and each of them individually or as a group are more closely related to HIV than are each individually or as a group related to BIV. In fact, CAEV, Visna and FIV form a cluster of closely related species.

As noted at pages 165 and 166 of the Virus Research article, the genomes of BIV and HIV are diverse and distinct. There are genes unique to BIV and unique to HIV. BIV is the most complex non-primate lentivirus characterized to date. Also in keeping with the intricate organization of the BIV genome, Gonda et al., teach that the transcriptional pattern of the BIV genome also is very complex.

At the top of 174 of the Gonda et al. article, it is noted that BIV, as with other lentiviruses, is species specific with respect to host cell infection. Thus, the tropism of BIV is very limited.

Hence, the Virus Research article supports the conclusions obtained from the '830 patent and the PCT, and which was known in the art, that BIV is very different from FIV, the lentiviruses have diverse genomes and the FIV vectors neither teach, suggest nor guide the making and using of BIV vectors to obtain transgene expression in human cells with a reasonable expectation of success.

The Examiner advanced the conclusion that the success of making FIV vectors suggests the making of vectors from other non-primate lentiviruses because the viruses are genetically related. A possible corollary of that position is that it is more likely to obtain vectors from viruses that are more closely related. Thus, one might predict that viruses more closely related to FIV can successfully yield vectors that can efficiently infect human cells and express a transgene therein.

Referring once again to Fig. 2 of the Gonda et al. article, note the phyletic relationship amongst the lentiviruses. It can be seen that Visna and CAEV are closely related to FIV and each in turn is more closely related to HIV than is BIV.

Attached hereto is a copy of Berkowitz et al., Virology, 279:116-129 (2001), who teach vectors made from Visna. As noted in the Abstract, specifically the last two sentences, while vectors were constructed, the vectors did not transduce target cells well. Thus, despite the high degree of genetic similarity between FIV and Visna, the success with FIV for making viral vectors that can infect human cells cannot be extrapolated to the closely related Visna virus.

Mselli-Lakhal et al., Arch. Virol., 143:681-695 (1998), copy attached hereto, teach making vectors from CAEV. Again, as noted in the Abstract, particularly the last few sentences thereof, vector titers were very low and overall transduction

efficiency was very low. Therefore, CAEV is another example of a lentivirus closely related to FIV where the making of vectors from FIV did not translate to making vectors from CAEV that successfully transduced human cells and efficiently expressed a transgene.

Therefore, two viruses very closely related to FIV did not yield usable viral vectors. The success with FIV cannot be extrapolated to even very closely related lentivirus such as CAEV and Visna.

The CAEV and Visna references support the position that the PCT application of Poeschia et al., WO 99/15641, provides at best, an invitation to experiment because there is no reasonable expectation of attaining vectors from any non-primate lentiviruses just because vectors were obtained from FIV. Evidence has proved that lentiviruses closely related to FIV do not yield usable viral vectors that express transgenes in human cells with high efficiency.

It follows then that there is no basis to conclude that the '830 patent and the published PCT application suggest the making of a BIV vector that efficiently expresses a transgene in human cells with a reasonable expectation of success. Accordingly, a prima facie case of obviousness over either the '830 patent, the PCT application or both has not been made.

Temin relates to BLV, which is not a lentivirus and thus, is unrelated to FIV, BIV and HIV. It follows then, that teachings relating to BLV are unlikely to be operable with BIV. Therefore, Temin does not cure the deficiencies of the '830 patent and the PCT application as to the instant application.

A prima facie case of obviousness over the three cited references has not been made.

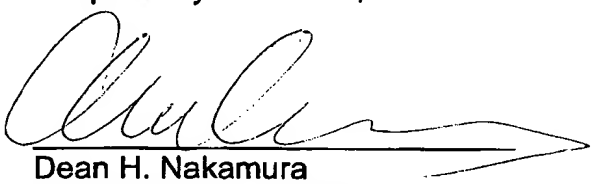
U.S. Ser. No. 09/734,836
Amendment Under 37 C.F.R. §1.116
June 28, 2004

Attached hereto is the Rule 132 Declaration of Dr. Sheila Connelly as one of ordinary skill in the art that based on the intricacies of BIV, the failed attempts of making vectors from non-primate lentiviruses and the differences of BIV from other lentiviruses, an artisan is not provided with adequate teaching and guidance in the cited references to make a successful BIV viral vector with a reasonable expectation of success.

In view thereof, withdrawal of the rejection is requested respectfully.

Reexamination, reconsideration, withdrawal of the rejection and early indication of allowance are solicited earnestly. If any issues remain, the Examiner is urged to contact the undersigned at the local exchange noted hereinbelow. If any additional fees are required, the Commission is authorized to charge Deposit Account No. 07-1896.

Respectfully submitted,



Dean H. Nakamura
Registration No. 33,981

GRAY CARY WARE & FREIDENRICH LLP
1625 Massachusetts Avenue, N.W.
Suite 300
Washington, D.C. 20036-2247
Telephone: (202) 238-7725
Facsimile: (202) 238-7701

Date: 28 June 2004